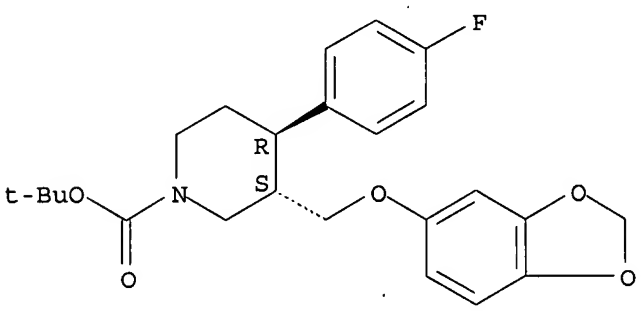
tartaric acid

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of paroxetine hydrochloride propanol solvate via human metabolite intermediate and characterization of solvate crystals)

RN 200572-35-6 CAPLUS

CN 1-Piperidinecarboxylic acid, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, 1,1-dimethylethyl ester, (3S,4R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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This file contains CAS Registry Numbers for easy and accurate substance identification.

tartaric acid

=> SET NOTICE DISPLAY 1

NOTICE SET TO 1 U.S. DOLLAR FOR DISPLAY COMMAND
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=> D ACC 133:4631 ALL

THE ESTIMATED COST FOR THIS REQUEST IS 7.06 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

ANSWER 1 CASREACT COPYRIGHT 2007 ACS on STN
AN 133:4631 CASREACT
TI Improved synthesis of paroxetine hydrochloride propan-2-ol solvate through one of metabolites in humans, and characterization of the solvate crystals
AU Sugi, Kiyoshi; Itaya, Nobushige; Katsura, Tadashi; Igi, Masami; Yamazaki, Shigeya; Ishibashi, Taro; Yamaoka, Teiji; Kawada, Yoshihiro; Tagami, Yayoi; Otsuki, Michiya; Ohshima, Takao
CS Central Research Laboratories, Sumika Fine Chemicals Co., Ltd., Osaka, 555-0021, Japan
SO Chemical & Pharmaceutical Bulletin (2000), 48(4), 529-536
CODEN: CPBTAL; ISSN: 0009-2363
PB Pharmaceutical Society of Japan
DT Journal
LA English
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
AB Paroxetine, a potent and selective inhibitor of 5-hydroxytryptamine (serotonin) uptake, was prepared through a piperidine derivative, which was reported to be one of the paroxetine metabolites in humans. Thus, the piperidine derivative was converted to its N-tert-butoxycarbonyl (N-Boc) derivative, which was then converted to N-Boc paroxetine. Paroxetine hydrochloride propan-2-ol (iso-Pr alc. (IPA)) solvate crystals were directly obtained from the N-Boc paroxetine by adding hydrogen chloride to the N-Boc paroxetine IPA solution The amount of IPA content in the crystals was reduced by drying with a continuous change of powder X-ray diffraction patterns. Other characterizations of the solvate crystals were also conducted.
ST paroxetine Paxil prepn; propanol paroxetine hydrochloride prepn; hemihydrate paroxetine hydrochloride prepn
IT 78246-49-8P 110429-35-1P, Paroxetine hydrochloride hemihydrate 181237-68-3P, 2-Propanol compound with (3S,4R)-3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)piperidine hydrochloride
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation of paroxetine hydrochloride propanol solvate via human metabolite intermediate and characterization of solvate crystals)
IT 105-34-0, Methyl cyanoacetate 459-57-4, 4-Fluorobenzaldehyde 533-31-3, 1,3-Benzodioxol-5-ol 34619-03-9, Di-tert-butyl carbonate 271595-66-5, Paroxetine L-o-chlorotartranilic acid salt
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of paroxetine hydrochloride propanol solvate via human metabolite intermediate and characterization of solvate crystals)
IT 125224-43-3P, (3S,4R)-(-)-4-(4-Fluorophenyl)-3-piperidinemethanol 188869-26-3P, (3R,4S)-rel-4-(4-Fluorophenyl)-3-piperidinemethanol 200572-35-6P, (3S,4R)-3-[(1,3-Benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-1-piperidinecarboxylic acid 1,1-dimethylethyl ester 200572-36-7P, 2-Cyano-3-(4-fluorophenyl)pentanedioic acid dimethyl ester 200572-37-8P, (3R,4S)-rel-4-(4-Fluorophenyl)-6-oxo-3-piperidinecarboxylic acid methyl ester 200572-39-0P, 4-(4-Fluorophenyl)-6-oxo-3-piperidinecarboxylic acid methyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

tartaric acid

(Reactant or reagent)
(preparation of paroxetine hydrochloride propanol solvate via human metabolite intermediate and characterization of solvate crystals)

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Amat, M; Tetrahedron: Asymmetry 1996, V7, P1591 CAPLUS
(2) Anon; Drugs Fut 1986, V11, P112
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(4) Barnes, R; Eur Pat Appl EP 223403 1987
(5) Buxton, P; Int J Pharm 1988, V42, P135 CAPLUS
(6) Christensen, J; 1974 CAPLUS
(7) Christensen, J; DE 2404113 1974 CAPLUS
(8) Haddock, R; Acta Psychiatr Scand 1989, V80(supp 350), P24
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(10) Hansen, J; PCT Int Appl WO 96 36636 1996
(11) Koelsch, C; J Am Chem Soc 1943, V65, P2459 CAPLUS
(12) Montzka, T; J O Chem 1968, V33, P3393
(13) Patil, V; Indian Drugs 1998, V35, P686 CAPLUS
(14) Sugi, K; 1998 CAPLUS
(15) Sugi, K; Eur Pat Appl EP 812827 1997
(16) Wang, S; 1997 CAPLUS
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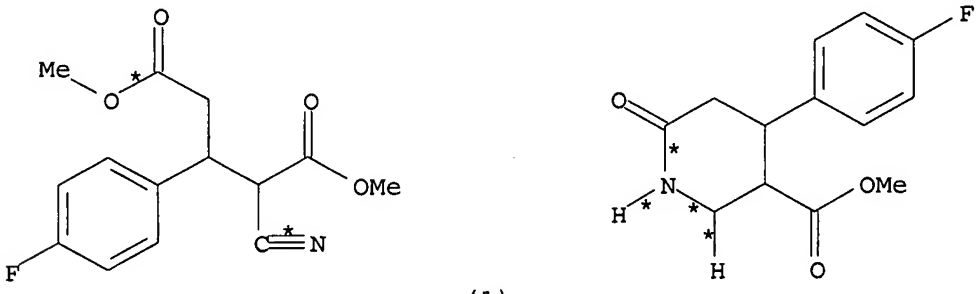
(20) Ward, N; DE 19603797 1996 CAPLUS
(21) Yokota, M; Bull Chem Soc 1999, V72, P1731 CAPLUS

RX(1) OF 15 ...A ===> B...



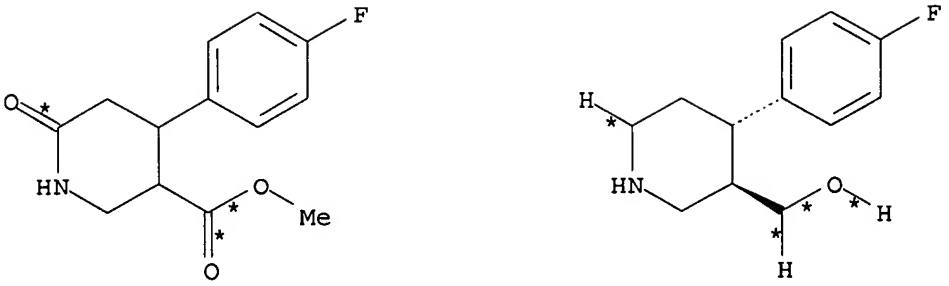
A

B
YIELD 90%

RX(1) RCT A 200572-36-7
RGT C 1333-74-0 H2
PRO B 200572-39-0
CAT 7440-02-0 Ni
SOL 67-56-1 MeOH, 108-88-3 PhMe

RX(2) OF 15 ...B ===> G...

tartaric acid



B

(2)

G
YIELD 83%

RX(2) RCT B 200572-39-0

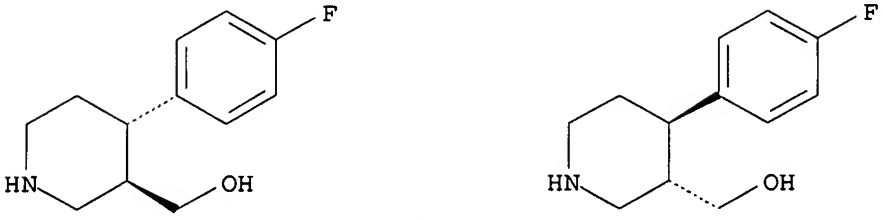
STAGE(1)
RGT H 124-41-4 NaOMe
SOL 108-88-3 PhMe

STAGE(2)
RGT I 16853-85-3 LiAlH4
SOL 109-99-9 THF

STAGE(3)
RGT J 1310-73-2 NaOH

PRO G 188869-26-3
NTE STEREOSELECTIVE

RX(3) OF 15 ...G ===> L...



G

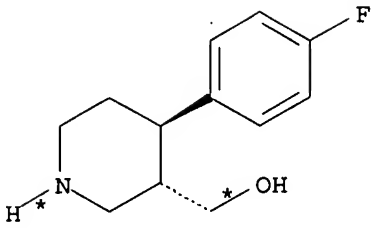
(3)

L
YIELD 39%

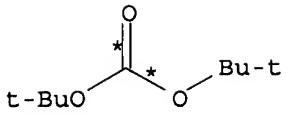
RX(3) RCT G 188869-26-3
RGT M 17447-35-7 Butanoic acid, 4-[(4-chlorophenyl)amino]-2,3-dihydroxy-4-oxo-, (2R,3R)-
PRO L 125224-43-3
SOL 7732-18-5 Water
NTE STEREOSELECTIVE

RX(4) OF 15 ...L + O + P ===> Q

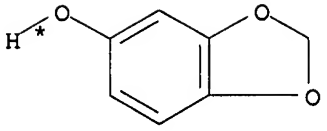
tartaric acid



L

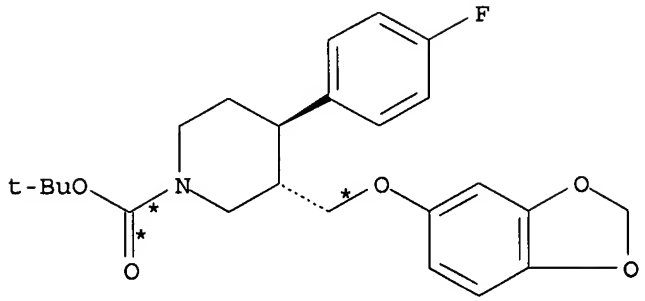


O



P

(4)



Q
YIELD 87%

RX(4) RCT L 125224-43-3, O 34619-03-9

STAGE(1)
RGT J 1310-73-2 NaOH
SOL 7732-18-5 Water,. 108-88-3 PhMe

STAGE(2)
RGT R 121-44-8 Et3N, S 98-59-9 TsCl
SOL 108-88-3 PhMe

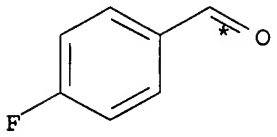
STAGE(3)
RCT P 533-31-3
RGT J 1310-73-2 NaOH, H 124-41-4 NaOMe

STAGE(4)
RGT T 7647-01-0 HCl, U 67-63-0 Me2CHOH
SOL 108-88-3 PhMe

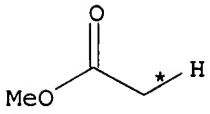
PRO Q 200572-35-6
NTE STEREOSELECTIVE

RX(5) OF 15 V + W + X ===> A...

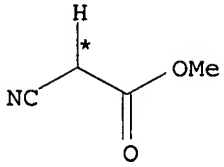
tartaric acid



V

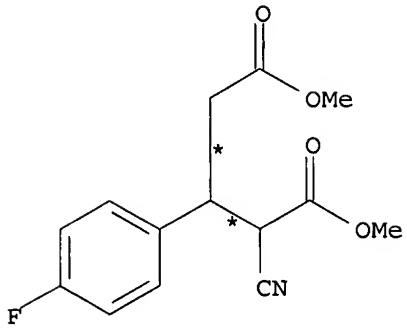


W



X

(5) →



A
YIELD 79%

RX(5) RCT V 459-57-4, W 79-20-9

STAGE(1)
RGT H 124-41-4 NaOMe
SOL 108-88-3 PhMe

STAGE(2)
RCT X 105-34-0

STAGE(3)
RGT T 7647-01-0 HCl
SOL 7732-18-5 Water

STAGE(4)
SOL 108-88-3 PhMe

PRO A 200572-36-7

tartaric acid

```
=> s paroxetine(l)buty?
          3333 PAROXETINE
        610983 BUTY?
L1          17 PAROXETINE(L)BUTY?

=> d bib hit 1-17

L1   ANSWER 1 OF 17  CAPLUS  COPYRIGHT 2007 ACS on STN
AN   2004:965034  CAPLUS
DN   141:400958
TI   Drug formulations with methacrylic acid-methylacrylate-ethylacrylate-
     butylmethacrylate copolymer containing coating or matrix
IN   Petereit, Hans-Ulrich; Meier, Christian; Schultes, Klaus
PA   Roehm G.m.b.H. & Co. K.-G., Germany
SO   PCT Int. Appl., 47 pp.
     CODEN: PIXXD2
DT   Patent
LA   German
FAN.CNT 2
     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
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PI   WO 2004096185        A1    20041111    WO 2004-EP2061          20040302
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
             ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
             SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
             TD, TG
     DE 10319458          A1    20041118    DE 2003-10319458        20030429
     CA 2489064           A1    20041111    CA 2004-2489064         20040302
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     BR 2004003949        A     20050301    BR 2004-3949            20040302
     CN 1697649           A     20051116    CN 2004-80000276        20040302
     JP 2006524643        T     20061102    JP 2006-504498          20040302
     IN 2004CN02444       A     20070907    IN 2004-CN2444          20040827
     US 2005152977        A1    20050714    US 2004-512860          20041115
PRAI DE 2003-10319458     A     20030429
     WO 2004-EP2061       W     20040302
RE.CNT  4      THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT   50-23-7, Hydrocortisone  50-24-8, Prednisolone  50-48-6, Amitriptyline
     50-52-2, Thioridazine  50-78-2, Acetylsalicylic acid  50-81-7,
     L-Ascorbic acid, biological studies  52-53-9, Verapamil  53-86-1,
     Indometacin  54-31-9, Furosemide  55-63-0, Glycerol trinitrate
     56-54-2, Quinidine  57-27-2, Morphin, biological studies  58-55-9,
     Theophylline, biological studies  67-20-9, Nitrofurantoin  70-47-3,
     Aspartamic acid, biological studies  71-63-6, Digitoxin  87-33-2,
     Isosorbide dinitrate  89-57-6, 5-Aminosalicylic acid  99-66-1, Valproic
     acid  100-97-0, biological studies  103-90-2, Paracetamol  113-92-8
     130-95-0, Quinine  151-21-3, Sodium lauryl sulfate, biological studies
     153-18-4, Rutoside  155-97-5, Pyridostigmine  298-46-4, Carbamazepin
     315-30-0, Allopurinol  317-34-0, Aminophyllin  364-62-5, Metoclopramide
     437-74-1, Xantinolnicotinate  479-92-5, Propyphenazone  525-66-6,
     Propranolol  599-79-1, Sulfasalazin  604-75-1, Oxazepam  1200-22-2,
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tartaric acid

Lipoic acid 1310-73-2, Sodium hydroxide, biological studies 2179-37-5, Bencyclane 2530-97-4, Xanthinol 2809-21-4 3737-09-5, Disopyramide 4498-32-2, Dibenzepine 4499-40-5, Choline theophyllinate 5104-49-4, Flurbiprofen 5636-83-9, Dimetindene 6452-71-7, Oxprenolol 6493-05-6, Pentoxifylline 6805-41-0, Aescin 7439-93-2, Lithium, biological studies 7439-93-2D, Lithium, salts 7440-09-7, Potassium, biological studies 7440-09-7D, Potassium, salts 7440-23-5, Sodium, biological studies 7440-23-5D, Sodium, salts 7440-66-6, Zinc, biological studies 7440-66-6D, Zinc, salts 7681-49-4, Sodium fluoride, biological studies 7681-93-8, Natamycin 8049-47-6, Pancreatin 9002-07-7, Trypsin 9002-64-6, Parathormone 9002-72-6, Somatotropin 9004-10-8, Insulin, biological studies 9006-65-9, Dimethicone 9007-12-9, Calcitonin 9007-92-5, Glucagon, biological studies 10596-23-3 11000-17-2, Vasopressin 13523-86-9, Pindolol 14838-15-4, Norephedrine 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 16051-77-7, Isosorbide mononitrate 16110-51-3, Cromolyn 16662-47-8, Gallopamil 16679-58-6 18559-94-9, Salbutamol 18683-91-5, Ambroxol 21829-25-4, Nifedipine 22071-15-4, Ketoprofen 22204-53-1, Naproxen 23031-25-6, Terbutalin 25717-80-0, Molsidomine 25812-30-0, Gemfibrozil 27203-92-5, Tramadol 29122-68-7, Atenolol 31329-57-4, Naftidrofuryl 40391-99-9 41575-94-4, Carboplatin 41859-67-0, Bezafibrate 42399-41-7, Diltiazem 49562-28-9, Fenofibrate 51110-01-1, Somatostatin 51333-22-3, Budesonide 51384-51-1, Metoprolol 53808-88-1, Lonazolac 55837-25-7, Buflomedil 55837-27-9, Piretanide 55985-32-5, Nicardipine 57132-53-3, Proglumetacin 61869-08-7, Paroxetine 63675-72-9, Nisoldipine 66085-59-4, Nimodipine 66376-36-1, Alendronate 73590-58-6, Omeprazole 74381-53-6, Leuprolide acetate 75330-75-5, Lovastatin 77337-73-6, Acamprosate calcium 79902-63-9, Simvastatin 81093-37-0, Pravastatin 88150-42-9, Amlodipine 89662-30-6, Detirelix 93413-69-5, Venlafaxine 93957-54-1, Fluvastatin 98530-12-2, Intron A 102625-70-7, Pantoprazole 103577-45-3 114084-78-5, Ibandronate 117976-89-3, Rabeprazole 119141-88-7, Esomeprazole 120287-85-6, Cetrorelix 134523-00-5, Atorvastatin 143011-72-7, Granulocyte Colony Stimulating factor 145599-86-6, Cerivastatin 150977-36-9, Bromelain 161973-10-0, Perprazole
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug formulations with methacrylic acid-methylacrylate-ethylacrylate-butylmethacrylate copolymer containing coating or matrix)

L1 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:299547 CAPLUS
DN 140:331639
TI Trends in the development of new antidepressants. Is there a light at the end of the tunnel?
AU Pacher, Pal; Kecskemeti, Valeria
CS National Institute on Alcohol Abuse & Alcoholism, Laboratory of Physiologic Studies, National Institutes of Health, Rockville, MD, 20852, USA
SO Current Medicinal Chemistry (2004), 11(7), 925-943
CODEN: CMCHE7; ISSN: 0929-8673
PB Bentham Science Publishers Ltd.
DT Journal; General Review
LA English
RE.CNT 226 THERE ARE 226 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB A review. Since the introduction of tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs) in mid-1950's, treatment of depression was dominated by monoamine hypotheses. The well-established clin. efficacy of TCAs and MAOIs is due, at least in part, to the enhancement of noradrenergic or serotonergic mechanisms, or to both. Unfortunately, their very broad mechanisms of action also include many unwanted effects related to their potent activity on cholinergic,

tartaric acid

adrenergic, and histaminergic receptors. The introduction of selective serotonin reuptake inhibitors (SSRIs) over twenty years ago had been the next major step in the evolution of antidepressants to develop drugs as effective as the TCAs but of higher safety and tolerability profile. During the past 2 decades SSRIs (fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram) gained incredible popularity and have become the most widely prescribed medication in the psychiatric practice. The evolution of antidepressants continued resulting in introduction of selective and reversible monoamine oxidase inhibitors (eg. moclobemid), selective noradrenaline (eg. reboxetine), dual noradrenaline and serotonin reuptake inhibitors (milnacipram, venlafaxin, duloxetin) and drugs with distinct neurochem. profiles such as mirtazapine, nefazadone, and tianeptine. Different novel serotonin receptor ligands were also intensively investigated. In spite of the remarkable structural diversity, most currently introduced antidepressants are "monoamine based". Furthermore, these newer agents are neither more efficacious nor rapid acting than their predecessors and approx. 30% of the population do not respond to current therapies. By the turn of the new millennium, the authors are all witnessing a result of innovative developmental strategies based on the better understanding of pathophysiol. of depressive disorder. Several truly novel concepts have emerged suggesting that the modulation of neuropeptide (substance P, corticotrophin-releasing factor, neuropeptide Y, vasopressin V1b, melanin-concentrating hormone-1), N-methyl-D-aspartate, nicotinic acetylcholine, dopaminergic, glucocorticoid, δ-opioid, cannabinoid and cytokine receptors, gamma-amino butyric acid (GABA) and intracellular messenger systems, transcription, neuroprotective and neurogenic factors, may provide an entirely new set of potential therapeutic targets, giving hope that further major advances might be anticipated in the treatment of depressive disorder soon. The goal of this review is to give a brief overview of the major advances from monoamine-based treatment strategies, and particularly focus on the new emerging approaches in the treatment of depression.

L1 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:111462 CAPLUS
DN 141:348856
TI Resolution of paroxetine precursor using different lipases Influence of the reaction conditions on the enantioselectivity of lipases
AU Fernandez-Lorente, Gloria; Palomo, Jose M.; Mateo, Cesar; Guisan, Jose M.; Fernandez-Lafuente, Roberto
CS Department of Biocatalysis, CSIC, Institute of Catalysis, Madrid, 28049, Spain
SO Enzyme and Microbial Technology (2004), 34(3-4), 264-269
CODEN: EMTED2; ISSN: 0141-0229
PB Elsevier Science
DT Journal
LA English
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB In this manuscript, lipases from different sources have been evaluated in the resolution of (±)-(4RS,5RS)-trans-5-(butyryloxymethyl)-4-(4'-fluorophenyl)-1-methyl-piperidin-2-one, an interesting precursor of paroxetine. Three of the analyzed lipases [Pseudomonas fluorescens (PFL), Candida antarctica form B (CAL-B) and Aspergillus oryze (AOL)] were selected for having the highest specific activity. It was found that slight changes on the reaction conditions greatly altered the lipases properties; for example the E value for PFL immobilized on octyl-Sepharose improved from 2 to 25 just by adding some organic solvent, being the (+)-trans-1 the preferred isomer. Moreover, the E value for the com. preparation of CAL-B could be altered from 2 to 18, favoring the (+)-trans-1 isomer. In the case of AOL, the E value could be improved

tartaric acid

from 3.5 to 16 in the presence of 20% dioxane. It is remarkable that this lipase presented the reverse enantiopreference compared to the other two lipases. Thus, good enantioselectivities could be achieved with the three enzymes, just by an appropriate engineering of the reaction medium.

L1 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:492188 CAPLUS
DN 139:77878
TI Preparation of tropanes, their rhenium and technetium chelates and use as radiopharmaceuticals and diagnostic agents
IN Turpin, Frederic; Mauclaire, Laurent; Masri, Fadi; Riche, Francoise; Du Moulinet D'Hardemare, Amaury
PA Schering Aktiengesellschaft, Germany
SO Fr. Demande, 65 pp.
CODEN: FRXXBL
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2833952	A1	20030627	FR 2001-16867	20011226
	FR 2833952	B1	20040326		
	WO 2003055879	A2	20030710	WO 2002-IB5357	20021213
	WO 2003055879	A3	20040617		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002367114	A1	20030715	AU 2002-367114	20021213
PRAI	FR 2001-16867	A	20011226		
	WO 2002-IB5357	W	20021213		

OS MARPAT 139:77878
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The present invention concerns tropanes (shown as I; variables defined below; e.g. II), their metal chelates with rhenium and technetium (e.g. Tc oxo and nitrido complexes with II), methods of preparation of the tropanes and their chelates, and uses as radiopharmaceuticals and diagnostic agents, e.g. visualization of reuptake of dopamine or serotonin. For I: X = a compound of chelation of a metal or a metal complex, carbons 6 and 7 being bonded or not; R1 is an alkyl or a alkenyl; R2 is COOZ (Z = H, alkyl); R3 = Ph, phenylalkyl or phenylalkenyl, benzoate or oxo; the connection between carbons 2 and 3 is a simple or double bond. The portions of X bonded to carbons 6 and 7 may be, for example, :NN(R7)CS2Me (R7 = H, Me). For example, II was prepared in a multistep synthesis starting from N-Bocpyrrole and (1S)-2-ethoxy-1-methyl-2-oxoethyl 3-(tert-butyldimethylsiloxy)-2-diazo-3-oxo-3-butenoate (prepns. described) involving the following intermediates: (1S)-2-ethoxy-1-methyl-2-oxoethyl (1R,5R)-8-[(1,1-dimethylethoxy)carbonyl]-3-(tert-butyldimethylsiloxy)-8-azabicyclo[3.2.1]octa-2,6-diene-2-carboxylate (shown as III, 75%), (1S)-2-ethoxy-1-methyl-2-oxoethyl (1R,5R)-8-[(1,1-dimethylethoxy)carbonyl]-8-azabicyclo[3.2.1]oct-6-en-3-one-2-carboxylate, (1S)-2-ethoxy-1-methyl-2-oxoethyl (1R,5R)-8-[(1,1-dimethylethoxy)carbonyl]-3-(trifluoromethanesulfonyloxy)-8-azabicyclo[3.2.1]octa-2,6-diene-2-carboxylate (22%), (1S)-2-ethoxy-1-methyl-2-oxoethyl (1R,5R)-8-[(1,1-dimethylethoxy)carbonyl]-3-(p-tolyl)-8-

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azabicyclo[3.2.1]octa-2,6-diene-2-carboxylate (33%), Me (1R,5R)-8-[(1,1-dimethylethoxy)carbonyl]-3-(p-tolyl)-8-azabicyclo[3.2.1]octa-2,6-diene-2-carboxylate (95%), Me (1R,2R,3R,5R)-8-[(1,1-dimethylethoxy)carbonyl]-3-(p-tolyl)-8-azabicyclo[3.2.1]oct-6-ene-2-carboxylate (85%), Me (1R,2R,3R,5R,6R,7R)-8-[(1,1-dimethylethoxy)carbonyl]-6,7-dihydroxy-3-(p-tolyl)-8-azabicyclo[3.2.1]octane-2-carboxylate (99%), and Me (1R,2R,3R,5R)-6-[(1,1-dimethylethoxy)carbonyl]-1,5-diformyl-3-(p-tolyl)-6-azacyclohexane-2-carboxylate (70%). Pharmacol. testing of Tc complexes of tropane derivs. yielded the following results: preinjection of GBR 12909 (specific inhibitor of dopamine transport) in rats prevented their fixation in the striatum; in vitro competitive studies on cerebral membranes with radiolabeled GBR 12925, paroxetine and nisoxetine showed the Tc complexes to have good affinity and specificity for dopamine transport; in vivo kinetic studies of cerebral distribution in a primate shows the complexes to be useful for visualization of dopamine transport; they pass the hemato-encephalic barrier and accumulate preferentially in the striatum with an elevated striatum/cerebellum ratio.

L1 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:58812 CAPLUS
DN 138:122554
TI Enzymic resolution of trans-4-(4-fluorophenyl)-3-hydroxymethylpiperidine derivative for optically pure paroxetine precursors
IN Bayod Jasanada, Miguel; Sanchez Pedregal, Victor; Gotor Santamaria, Vicente; Brieva Collado, Rosario; De Gonzalo Calvo, Gonzalo
PA Astur Pharma, Spain
SO U.S. Pat. Appl. Publ., 9 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003018048	A1	20030123	US 2002-192768	20020710
	ES 2194588	A1	20031116	ES 2001-1648	20010713
	ES 2194588	B1	20041016		
	EP 1283200	A2	20030212	EP 2002-380156	20020710
	EP 1283200	A3	20030305		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
PRAI	ES 2001-1648	A	20010713		

OS CASREACT 138:122554; MARPAT 138:122554
IT 108-88-3, Toluene, uses 141-78-6, Ethyl acetate, uses 1634-04-4, tert-Butyl methyl ether
RL: NUU (Other use, unclassified); USES (Uses)
(reaction solvent; enzymic resolution of trans(4-fluorophenyl)hydroxymethylpiperidine derivative for optically pure paroxetine precursors)

L1 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:28518 CAPLUS
DN 138:314796
TI Fox odor affects corticosterone release but not hippocampal serotonin reuptake and open-field behavior in rats
AU Dias Soares, Danusa; Fernandez, Francesca; Aguerre, Sylvie; Foury, Aline; Mormede, Pierre; Chaouloff, Francis
CS INSERM U471-INRA, Institut F. Magendie, Bordeaux, 33077, Fr.
SO Brain Research (2003), 961(1), 166-170
CODEN: BRREAP; ISSN: 0006-8993
PB Elsevier Science B.V.
DT Journal

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LA English
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB Group-housed Sprague-Dawley (SD) rats exposed for 1 h to 2,5-dihydro-2,4,5-trimethylthiazoline (TMT, a component of fox feces) did not display changes in hippocampal serotonin (5-HT) metabolism and [3H]5-HT reuptake, compared to water or butyric acid. Such an observation extended to isolated SD and Fischer 344 rats. When group-housed SD rats were tested 1 wk after a 1-h exposure to TMT, hippocampal 5-HT metabolism, [3H]5-HT reuptake, and [3H]paroxetine binding at the 5-HT transporter remained unchanged. This study questions TMT as a specific predatory stimulus as both butyric acid and TMT increased plasma corticosterone levels while leaving intact open-field behavior (at least in group-housed SD rats).

L1 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:676014 CAPLUS
DN 137:216939
TI Process of preparing paroxetine and intermediates for use therein
IN Callewaert, George Leo
PA Spurcourt Limited, UK
SO PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002068416	A2	20020906	WO 2002-GB771	20020222
	WO 2002068416	A3	20021121		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2438892	A1	20020906	CA 2002-2438892	20020222
	AU 2002232017	A1	20020912	AU 2002-232017	20020222
	EP 1362032	A2	20031119	EP 2002-712110	20020222
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2004073038	A1	20040415	US 2003-468865	20030820
PRAI	GB 2001-4583	A	20010224		
	GB 2001-25119	A	20011018		
	WO 2002-GB771	W	20020222		

OS MARPAT 137:216939
IT 501-53-1, Benzyl chloroformate 24424-99-5, Di-tert-butyl dicarbonate 66270-36-8, 2,2,2-Trichloro-1,1-dimethylethyl chloroformate
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation agent; process of preparing paroxetine and intermediates for use therein)
IT 74-89-5, Methylamine, reactions 75-04-7, Ethylamine, reactions 100-46-9, Benzylamine, reactions 104-84-7, 4-Methylbenzylamine 105-53-3, Diethyl malonate 109-73-9, Butylamine, reactions 109-85-3, 2-Methoxyethylamine 4795-29-3, Tetrahydrofurfurylamine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of starting materials; process of preparing paroxetine and intermediates for use therein)

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L1 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:310324 CAPLUS
DN 136:380004
TI Prolonged prenatal psychotropic medication exposure alters Neonatal acute pain response
AU Oberlander, Tim F.; Grunau, Ruth Eckstein; Fitzgerald, Colleen; Ellwood, Ann-Louise; Misri, Shaila; Rurak, Dan; Riggs, Kenneth Wayne
CS Department of Pediatrics, University of British Columbia, Vancouver, BC, V6H 3V4, Can.
SO Pediatric Research (2002), 51(4), 443-453
CODEN: PEREBL; ISSN: 0031-3998
PB Lippincott Williams & Wilkins
DT Journal
LA English
RE.CNT 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB Selective serotonin reuptake inhibitors (SSRIs) and benzodiazepines are frequently used to treat maternal depression during pregnancy, however the effect of increased serotonin (5HT) and γ-amino- butyric acid (GABA) agonists in the fetal human brain remains unknown. 5HT and GABA are active during fetal neurol. growth and play early roles in pain modulation, therefore, if prolonged prenatal exposure alters neurodevelopment this may become evident in altered neonatal pain responses. To examine biol. and behavioral effects of prenatal exposure, neonatal responses to acute pain (phenylketonuria heel lance) in infants with prolonged prenatal exposure were examined Facial action (Neonatal Facial Coding System) and cardiac autonomic reactivity derived from the relationship between respiratory activity and short term variations of heart rate (HRV) were compared between 22 infants with SSRI exposure (SE) [fluoxetine (n = 7), paroxetine (n = 11), sertraline (n = 4)]; 16 infants exposed to SSRIs and clonazepam (SE+) [paroxetine (n = 14), fluoxetine (n = 2)]; and 23 nonexposed infants during baseline, lance, and recovery periods of a heel lance. Length of maternal SSRI use did not vary significantly between exposure groups-[mean (range)] SE:SE+ 183 (31-281):141 (54-282) d ($p > 0.05$). Infants exposed to SE and SE+ displayed significantly less facial activity to heel lance than control infants. Mean HR increased with lance, but was significantly lower in SE infants during recovery. Using measures of HRV and the transfer relationship between heart rate and respiration, SSRI infants had a greater return of parasympathetic cardiac modulation in the recovery period, whereas a sustained sympathetic response continued in the control group. Prolonged prenatal SSRI exposure appears to be associated with reduced behavioral pain responses and increased parasympathetic cardiac modulation in recovery following an acute neonatal noxious event. Possible 5HT-mediated pain inhibition, pharmacol. factors and the developmental course remain to be studied.

L1 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2000:240402 CAPLUS
DN 133:4631
TI Improved synthesis of paroxetine hydrochloride propan-2-ol solvate through one of metabolites in humans, and characterization of the solvate crystals
AU Sugi, Kiyoshi; Itaya, Nobushige; Katsura, Tadashi; Igi, Masami; Yamazaki, Shigeya; Ishibashi, Taro; Yamaoka, Teiji; Kawada, Yoshihiro; Tagami, Yayoi; Otsuki, Michiya; Ohshima, Takao
CS Central Research Laboratories, Sumika Fine Chemicals Co., Ltd., Osaka, 555-0021, Japan
SO Chemical & Pharmaceutical Bulletin (2000), 48(4), 529-536
CODEN: CPBTAL; ISSN: 0009-2363
PB Pharmaceutical Society of Japan
DT Journal
LA English

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OS CASREACT 133:4631
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT 105-34-0, Methyl cyanoacetate 459-57-4, 4-Fluorobenzaldehyde 533-31-3, 1,3-Benzodioxol-5-ol 34619-03-9, Di-tert-butyl carbonate 271595-66-5, Paroxetine L-o-chlorotartranilic acid salt
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of paroxetine hydrochloride propanol solvate via human metabolite intermediate and characterization of solvate crystals)

L1 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1999:94050 CAPLUS
DN 130:320701
TI Psychopharmacological profile of the selective serotonin reuptake inhibitor, paroxetine: implication of noradrenergic and serotonergic mechanisms
AU Redrobe, John P.; Bourin, Michel; Colombel, Marie Claude; Baker, Glen B.
CS GIS Medicament, JE 2027 Neurobiologie de l'anxiete, Faculte de Medecine, Nantes, 44035, Fr.
SO Journal of Psychopharmacology (London) (1998), 12(4), 348-355
CODEN: JOPSEQ; ISSN: 0269-8811
PB SAGE Publications
DT Journal
LA English
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB The present study was designed to evaluate the psychopharmacol. profile of the selective serotonin reuptake inhibitor paroxetine, and thus assess potential noradrenergic and/or serotonergic activity. Paroxetine dose-dependently increased mobility time in the mouse forced swimming test (8, 16, 32 and 64 mg/kg, i.p.) and reduced spontaneous locomotor activity when administered at a high dose (64 mg/kg, i.p.). Prior administration of 8-hydroxy-2-(di-n-propylamino)tetralin (1 mg/kg, i.p.), (±) pindolol (32 mg/kg, i.p.) or 5-methoxy-3-(1,2,3,6-tetrahydro-4-pyridyl)-1H-indole (RU 24969) (1 mg/kg, i.p.) potentiated the antidepressant-like effects of subactive doses of paroxetine (1, 2 and 4 mg/kg, i.p.) in the mouse forced swimming test. These effects were antagonized by prior administration of 1-(2-methoxyphenyl)-4-[-(2-phthalimido)butyl]piperazine) (0.5 mg/kg, i.p.). Complementary studies suggested that RU24969-induced anti-immobility effects were a result of an increase in locomotor activity; other interactions were without increase/decrease in locomotor activity. Acute administration of paroxetine (8, 16, and 32 mg/kg, i.p.) antagonized the hypothermia induced by the D2/D1 receptor agonist, apomorphine (16 mg/kg, s.c.), while repeated treatment with paroxetine (32 mg/kg) attenuated clonidine-induced (0.5 mg/kg, i.p.) hypothermia. Pre-treatment with the serotonergic neurotoxin, para-chlorophenylalanine attenuated the anti-immobility effects of low doses of paroxetine (8 and 16 mg/kg, i.p.) in the forced swimming test, whereas a higher dose of paroxetine remained active (32 mg/kg, i.p.). The results of the present study indicated that paroxetine displayed both noradrenergic-like and serotonergic-like activity in the pre-clin. psychopharmacol. tests employed.

L1 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1999:74285 CAPLUS
DN 130:261951
TI N-tert-butyl-alpha-phenylnitrone protects against 3,4-methylenedioxymethamphetamine-induced depletion of serotonin in rats
AU Yeh, S. Y.
CS Molecular Neuropsychiatry Section, Intramural Research Program, National Institute on Drug Abuse, National Institutes of Health, Baltimore, MD,

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21224, USA
SO Synapse (New York) (1999), 31(3), 169-177
CODEN: SYNAET; ISSN: 0887-4476
PB Wiley-Liss, Inc.
DT Journal
LA English
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB The present study examined the effect of N-tert-butyl -alpha-phenylnitrone (PBN) on 3,4-methylenedioxymethamphetamine (MDMA)-induced depletion of serotonin in the CNS. Rats were treated with two concurrent injections of MDMA (20 mg/kg, s.c.), PBN (50-400 mg/kg dissolved in ethanol, 50 mg/mL of 25% ethanol, i.p.), saline or 25% ethanol, alone or in combination, 6 h apart, and sacrificed 5 days later. Rectal temperature was measured prior to and hourly following the drug injection for 5 h. Monoamine levels in the tissue were measured by HPLC. D. of the 5-HT transporters was assayed by [3H]paroxetine binding. Rectal temperature of rats increased after MDMA, decreased after PBN, ethanol, PBN plus ethanol, and MDMA plus ethanol, and was not significantly altered after MDMA plus PBN. Levels of 5-HT and 5-HIAA in the frontal cortex, hippocampus, striatum, and brain stem of rats decreased significantly after MDMA or MDMA plus ethanol, but not after MDMA plus PBN, PBN plus ethanol (PBN dissolved in ethanol), or ethanol as compared to the saline controls. Levels of 5-HT and 5-HIAA in the brain tissues of rats treated with MDMA plus PBN were elevated as compared to those treated with MDMA plus saline. Similar results were observed in the d. of 5-HT transporters in the frontal cortex and hippocampus. These results indicate that scavenging of free radicals of MDMA metabolites or reactive oxygen species by PBN and with lowering of body temperature protected against MDMA-induced depletion of serotonin transmitter.

L1 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1998:579448 CAPLUS
DN 130:371
TI Discriminative stimulus properties of the 5-HT1A receptor agonist BAY x 3702 in the rat
AU De Vry, Jean; Jentzsch, Klaus Rudiger
CS CNS Research, Bayer, Cologne, D-51063, Germany
SO European Journal of Pharmacology (1998), 357(1), 1-8
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB The aminomethylchroman derivative BAY x 3702 (R-(-)-2-{4-[(chroman-2-ylmethyl)-amino]-butyl}-1,1-dioxo-benzo[d]isothiazolone HCl) has recently been characterized as a relatively selective, high affinity 5-HT1A receptor agonist with neuroprotective, anxiolytic- and antidepressant-like effects in animal models. It was the aim of the present study to further confirm its receptor binding profile in an in vivo assay. Rats were trained to discriminate BAY x 3702 (0.1 mg/kg, i.p.) from vehicle in a standard two-lever fixed ratio 10 food-reinforced procedure. All rats learned the discrimination, the median number of sessions to reach criterion being 38 (range: 22-58 sessions). Generalization tests with BAY x 3702 showed dose-dependent and complete generalization after different routes of administration; the ED50 values being: 0.030, 0.007 and 0.36 mg/kg, after i.p., i.v. and p.o. administration, resp. Assessment of the duration of action after administration of 0.1 mg/kg BAY x 3702, i.p., resulted in a T1/2 of 65 min. Dose-dependent and complete generalization was also

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obtained with the 5-HT1A receptor agonists 8-OH-DPAT (8-hydroxy-2-(di-n-propylamino)-tetralin, ED50 in mg/kg, i.p.: 0.086), flesinoxan (0.30), SR 57746A (4-(3-trifluoromethylphenyl)-N-(2-(naphth-2-yl)ethyl)-1,2,3,6-tetrahydropyridine HCl, 1.0), the (+)-enantiomer of BAY x 3702 (1.3) and ipsapirone (1.8); the ED50 values being closely correlated with their resp. affinities for the 5-HT1A receptor. Pretreatment with the selective 5-HT1A receptor antagonist WAY-100635 ((N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-N(2-pyridinyl) cyclohexane carboxamide trihydrochloride) dose-dependently and completely blocked the discriminative effects of 0.1 mg/kg BAY x 3702 (ID50: 0.013 mg/kg, i.p.). WAY-100635, prazosin, idazoxan, raclopride, paroxetine, (-)-BAY k 8644 (methyl-1,4-dihydro-2,6-dimethyl-3-nitro-4-(2-trifluoro-methyl-phenyl)-pyridine-5-carboxylate), ethanol, and the putative neuroprotectants MK-801 ((+)-5-methyl-10,11-dihydroxy-5H-dibenzo(a,d)cyclohepten-5,10-imine), CNS 1102 (N-(1-naphthyl)-N'-(3-ethylphenyl)-N'-methyl-guanidine), CGS 19755 (cis-4-(phosphonomethyl) piperidine-2-carboxylic acid) and nimodipine did not induce more than 20% generalization. It is concluded that the BAY x 3702 cue is mediated by its agonistic activity at 5-HT1A receptors.

L1 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1998:250464 CAPLUS
DN 129:12626
TI Pindolol does not act only on 5-HT1A receptors in augmenting antidepressant activity in the mouse forced swimming test
AU Bourin, Michel; Redrobe, John P.; Baker, Glen B.
CS GIS Medicament, JE 2027 Neurobiologie de l'Anxiete, Faculte de Medicine, Nantes, F-44035, Fr.
SO Psychopharmacology (Berlin) (1998), 136(3), 226-234
CODEN: PSCHDL; ISSN: 0033-3158
PB Springer-Verlag
DT Journal
LA English
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB The present study was undertaken to identify the receptor subtypes involved in (±) pindolol's ability to enhance the effects of antidepressant drugs in the mouse forced swimming test. Interaction studies were performed with S 15535 (presynaptic 5-HT1A receptor agonist) and methiothepin (5-HT1B autoreceptor antagonist) to attenuate or potentiate antidepressant-like activity. (±) Pindolol was tested in combination with selective agonists and antagonists at 5-HT1, 5-HT2 and 5-HT3 receptor subtypes. Pretreatment with S 15535 and methiothepin attenuated the activity of paroxetine, fluvoxamine and citalopram (32 mg/kg, IP; $P < 0.01$). (±) Pindolol (32 mg/kg, IP) induced significant anti-immobility effects when tested in combination with 5-methoxy-3-(1,2,3,6-tetrahydro-4-pyridyl)-1H-indole (RU 24969) (1 mg/kg, IP; $P < 0.05$), 1-(2-methoxyphenyl)-4-[-(2-phthalimido) butyl]piperazine (NAN 190) (0.5 mg/kg; $P < 0.05$) and ondansetron (0.00001 mg/kg, IP; $P < 0.01$). Pretreatment with NAN 190 (0.5 mg/kg, IP) potentiated the effects of RU 24969 (1 mg/kg, IP; $P < 0.05$) and (±) pindolol (32 mg/kg, IP; $P < 0.05$) in the forced swimming test, as did ondansetron (0.00001 mg/kg, IP). Significant additive effects were induced when RU 24969 (1 mg/kg, IP) was tested in combination with NAN 190 (0.5 mg/kg, IP; $P < 0.05$), (±) pindolol (32 mg/kg, IP; $P < 0.05$) and ondansetron (0.0000 mg/kg, IP; $P < 0.05$). 8-Hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT) (1 mg/kg, IP) or ketanserin (8 mg/kg, IP) did not induce significant antidepressant-like effects with any of the agonists/antagonists tested. The results of the present study suggest that pindolol is acting at presynaptic 5-HT1B serotonergic receptors, in addition to the 5-HT1A subtype, in augmenting the activity of antidepressants in the mouse forced swimming test.

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L1 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1998:13682 CAPLUS
DN 128:75308
TI Preparation of piperidine derivative as intermediates for the preparation of paroxetine
IN Sugi, Kiyoshi; Itaya, Nobushige; Katsura, Tadashi; Igi, Masami; Yamazaki, Shigeya; Ishibashi, Taro; Yamaoka, Teiji; Kawada, Yoshihiro; Tagami, Yayoi
PA Sumika Fine Chemicals Co., Ltd., Japan
SO Eur. Pat. Appl., 37 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 812827	A1	19971217	EP 1997-303647	19970529
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL, SE				
	JP 10291975	A	19981104	JP 1997-145833	19970519
	JP 3819532	B2	20060913		
	EP 1384711	A1	20040128	EP 2003-77856	19970529
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL, SE				
	EP 1384720	A1	20040128	EP 2003-77858	19970529
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL, SE				
	EP 1394160	A1	20040303	EP 2003-77857	19970529
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL, SE				
	IN 1997MA01172	A	20050304	IN 1997-MA1172	19970602
	US 5948914	A	19990907	US 1998-53653	19980402
	US 6476227	B1	20021105	US 2000-550175	20000414
	US 6610851	B1	20030826	US 2000-695383	20001025
	US 2003144519	A1	20030731	US 2003-336678	20030106
	US 6815548	B2	20041109		
PRAI	JP 1996-175893	A	19960613		
	JP 1996-294585	A	19961015		
	JP 1996-303838	A	19961029		
	JP 1996-326177	A	19961120		
	JP 1997-50980	A	19970218		
	EP 1997-303647	A3	19970529		
	US 1997-871948	A3	19970610		
	US 1999-306411	B3	19990506		
	US 2000-695383	A3	20001025		

OS MARPAT 128:75308
IT 105-34-0, Methyl cyanoacetate 124-63-0, Methanesulfonyl chloride 459-57-4, p-Fluorobenzaldehyde 501-53-1, Benzyl chloroformate 533-31-3, 3,4-Methylenedioxyphenol 24424-99-5, Di-tert-butyl dicarbonate 96426-60-7, Methyl p-fluorocinnamate 109887-53-8 125224-43-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of piperidine derivative as intermediates for the preparation of paroxetine)

L1 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1996:215542 CAPLUS
DN 125:11185
TI Synthesis of homochiral piperidine derivatives from S-glutamic acid. Stereoselective 1,4-addition of organocuprates to a Δ3-piperidine-2-one. A paroxetine analog
AU Herdeis, Claus; Kaschinski, Claudia; Karia, Rolf; Lotter, Hermann
CS Inst. Pharmazie Lebensmittelchemie Univ., Wuerzburg, 97074, Germany
SO Tetrahedron: Asymmetry (1996), 7(3), 867-84
CODEN: TASYE3; ISSN: 0957-4166

tartaric acid

PB Elsevier
DT Journal
LA English
OS CASREACT 125:11185
IT 352-13-6, 4-Fluorophenylmagnesium bromide 591-51-5, Phenyllithium
693-03-8, Butylmagnesium bromide 873-77-8,
4-Chlorophenylmagnesium bromide 917-64-6, Methylmagnesium iodide
1730-25-2, Allylmagnesium bromide 10467-10-4, Ethylmagnesium iodide
20850-43-5, Piperonyl chloride 24211-54-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of homochiral piperidine derivs. from S-glutamic acid via stereoselective 1,4-addition of organocuprates to a Δ3-piperidine-2-one in preparation of paroxetine analog)

L1 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1994:595833 CAPLUS
DN 121:195833
TI Antidepressant-induced modulation of GABAA receptors and β-adrenoceptors but not GABAB receptors in the frontal cortex of olfactory bulbectomized rats
AU Dennis, Trevor; Beauchemin, Valerie; Lavoie, Normand
CS Neurobiological Psychiatry Unit, McGill University, Department of Psychiatry, 1033 Pine Avenue West, Montreal, Quebec, Can.
SO European Journal of Pharmacology (1994), 262(1-2), 143-8
CODEN: EJPHAZ; ISSN: 0014-2999
DT Journal
LA English
AB The effects of prolonged administration of antidepressant drugs, belonging to three different classes, on high-affinity GABAA receptor, GABAB receptor and β-adrenoceptor binding parameters were determined in the frontal cortex of olfactory bulbectomized rats. Clorgyline (1 mg/kg/day), paroxetine (10 mg/kg/day) or desipramine (10 mg/kg/day) were administered for 21 days via s.c. osmotic minipumps implanted in the scapular region 7 days after bulbectomy. Cortical GABAA receptor densities, defined with [3H]γ-aminobutyric acid ([3H]GABA), were significantly increased following bulbectomy. This effect on Bmax values was reversed by all three antidepressant drugs. GABAB receptor densities decreased slightly after bulbectomy. Chronic antidepressant administration had no effect on GABAB receptor binding parameters. Olfactory bulbectomy did not induce any changes in cortical β-adrenoceptor binding parameters determined with [3H]CGP-12177 ((-)-4-(3-t-butylamino-2-hydroxypropoxy)- [5,7-3H]benzimidazol-2-one). However, prolonged administration of all three antidepressant drugs induced a downregulation of β-adrenoceptors. The results of the present study confirm the involvement of cortical GABAA rather than GABAB receptors in the olfactory bulbectomy animal model of human depression. Moreover, the data further support the hypothesis that a decrease in function of the GABAA receptor complex could play a role in the therapeutic effects of antidepressant treatments.

L1 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1994:525100 CAPLUS
DN 121:125100
TI Further evidence for the importance of 5-HT1A autoreceptors in the action of selective serotonin reuptake inhibitors
AU Hjorth, Stephan; Auerbach, Sidney B.
CS Department of Pharmacology, University of Goeteborg, Goteborg, Swed.
SO European Journal of Pharmacology (1994), 260(2-3), 251-5
CODEN: EJPHAZ; ISSN: 0014-2999
DT Journal
LA English
AB The clin. efficacy of antidepressants that block serotonin

tartaric acid

(5-hydroxytryptamine, 5-HT) reuptake may be restrained by indirect activation of autoreceptors. In vivo microdialysis in rat hippocampus was used to assess the release-inhibitory properties of the 5-HT reuptake inhibitors citalopram and paroxetine. When reuptake was first blocked by infusing citalopram into the hippocampus, systemic administration of citalopram or paroxetine resulted in a 50-70% decrease in hippocampal 5-HT overflow. This presumably reflected the inhibition of 5-HT release subsequent to reuptake blockade in the raphe nuclei and, in turn, activation of somatodendritic autoreceptors. In support, pretreatment with (±)-pindolol or (+)-WAY100135 ((+)-N-tert-butyl-3-(4-(2-methoxyphenyl)piperazine-1-yl)-2-phenylpropanamide dihydrochloride), to block 5-HT1A autoreceptors, abolished the decrease in 5-HT produced by systemic injection of the uptake blockers.

tartaric acid

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=> s wo2004026861/pn
L2            1 WO2004026861/PN
                (WO2004026861/PN)

=> d bib abs

L2   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2007 ACS on STN
AN   2004:267324  CAPLUS
DN   140:287369
TI   Process for producing paroxetine hydrochloride hydrate
IN   Yamazaki, Shigeya; Yoshikawa, Taichi
PA   Sumika Fine Chemicals Co., Ltd., Japan
SO   PCT Int. Appl., 18 pp.
     CODEN: PIXXD2
DT   Patent
LA   Japanese
FAN.CNT 2
     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
PI   WO 2004026861         A1    20040401    WO 2003-JP11806         20030917 <--
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG,
             PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR,
             TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2496727             A1    20040401    CA 2003-2496727         20030917
     AU 2003271056          A1    20040408    AU 2003-271056          20030917
     EP 1555263             A1    20050720    EP 2003-751271          20030917
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     BR 2003014596          A     20050809    BR 2003-14596           20030917
     US 2006041138          A1    20060223    US 2005-527337          20050310
PRAI JP 2002-273901         A     20020919
     JP 2002-288640         A     20021001
     WO 2003-JP11806        W     20030917
AB   This document discloses a process for producing paroxetine hydrochloride
     hydrate (I), which comprises reacting (3S,4R)-1-tert-butoxycarbonyl-4-(4-
     fluorophenyl)-3-[(3,4-methylenedioxy)phenoxymethyl]piperidine with
     hydrogen chloride in the presence of water and then precipitating crystals in
the
     presence of water.  Also claimed is a pharmaceutical composition containing I
for
     treatment of a variety of mental disorders.
RE.CNT  15    THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> analyze l2
ENTER ANSWER NUMBER OR RANGE (1-):1
ENTER DISPLAY CODE (TI) OR ?:rn
L3          ANALYZE L2 1 RN :       5 TERMS

=> fil reg
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                                                      ENTRY     SESSION
FULL ESTIMATED COST                                   16.51       62.64
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tartaric acid

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE ENTRY TOTAL SESSION

CA SUBSCRIBER PRICE -0.78 -9.36

FILE 'REGISTRY' ENTERED AT 12:41:50 ON 13 NOV 2007
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 12 NOV 2007 HIGHEST RN 953132-99-5
DICTIONARY FILE UPDATES: 12 NOV 2007 HIGHEST RN 953132-99-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

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Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

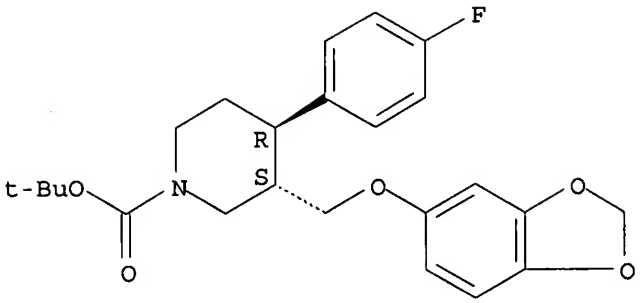
=> s l3
L4 5 L3

=> d 1-5

L4 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2007 ACS on STN
RN 200572-35-6 REGISTRY
ED Entered STN: 29 Jan 1998
CN 1-Piperidinecarboxylic acid, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, 1,1-dimethylethyl ester, (3S,4R)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1-Piperidinecarboxylic acid, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, 1,1-dimethylethyl ester, (3S-trans)-
OTHER NAMES:
CN (3S,4R)-3-[(1,3-Benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-1-piperidinecarboxylic acid 1,1-dimethylethyl ester
FS STEREOSEARCH
MF C24 H28 F N O5
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).

tartaric acid



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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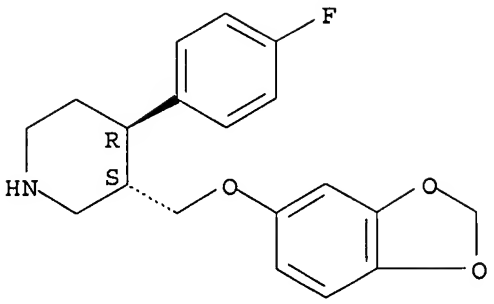
13 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L4 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2007 ACS on STN
RN 110429-35-1 REGISTRY
ED Entered STN: 27 Sep 1987
CN Piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, hydrochloride, hydrate (2:2:1), (3S,4R)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, hydrochloride, hydrate (2:1), (3S-trans)-
CN Piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, hydrochloride, hydrate (2:1), (3S,4R)- (9CI)
OTHER NAMES:
CN (-)-trans-4-(4-Fluorophenyl)-3-(3,4-methylenedioxyphenoxymethyl)piperidine hydrochloride hemihydrate
CN Paroxetine hydrochloride hemihydrate
FS STEREOSEARCH
MF C19 H20 F N O3 . Cl H . 1/2 H2 O
CI COM
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, IMSPATENTS, IMSRESEARCH, MRCK*, PS, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
CRN (61869-08-7)

Absolute stereochemistry. Rotation (-).

tartaric acid



● HCl

● 1/2 H_2O

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

58 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
58 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L4 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2007 ACS on STN
RN 7732-18-5 REGISTRY
ED Entered STN: 16 Nov 1984
CN Water (CA INDEX NAME)
OTHER NAMES:
CN Aquafina
CN Distilled water
CN DRiWATER
CN Hydrogen oxide (H2O)
CN NSC 147337
CN R 718
CN Spa
DR 558440-22-5, 558440-53-2
MF H2 O
CI COM
LC STN Files: ANABSTR, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CSCHEM, CSNB, DETHERM*, EMBASE, GMELIN*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, PIRA, PROMT, RTECS*, SCISEARCH, SPECINFO, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

H_2O

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

398819 REFERENCES IN FILE CA (1907 TO DATE)
1380 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

tartaric acid

399673 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L4 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2007 ACS on STN
RN 7647-01-0 REGISTRY
ED Entered STN: 16 Nov 1984
CN Hydrochloric acid (CA INDEX NAME)
OTHER NAMES:
CN Anhydrous hydrochloric acid
CN Baume HCL
CN Chloridric acid
CN Chlorohydric acid
CN Dilute hydrochloric acid
CN Enplate PO 236
CN Hydrochloric acid gas
CN Hydrogen chloride
CN Hydrogen chloride (HCl)
CN Muriatic acid
CN NSC 77365
DR 113962-65-5, 51005-19-7, 61674-62-2, 218625-68-4
MF Cl H
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DETHERM*, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, TULSA, ULIDAT, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

HCl

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

105978 REFERENCES IN FILE CA (1907 TO DATE)
654 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
106663 REFERENCES IN FILE CAPLUS (1907 TO DATE)
40 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L4 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2007 ACS on STN
RN 108-88-3 REGISTRY
ED Entered STN: 16 Nov 1984
CN Benzene, methyl- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Toluene (8CI)
OTHER NAMES:
CN 1-Methylbenzene
CN Antisal 1a
CN CP 25
CN CP 25 (solvent)
CN Methacide
CN Methylbenzene
CN Methylbenzol
CN NSC 406333
CN Phenylmethane
CN Toluol
MF C7 H8
CI COM

tartaric acid

LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, PIRA, PROMT, PS, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TULSA, ULIDAT, USPAT2, USPATFULL, VETU
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Other Sources: DSL**, EINECS**, TSCA**
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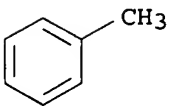

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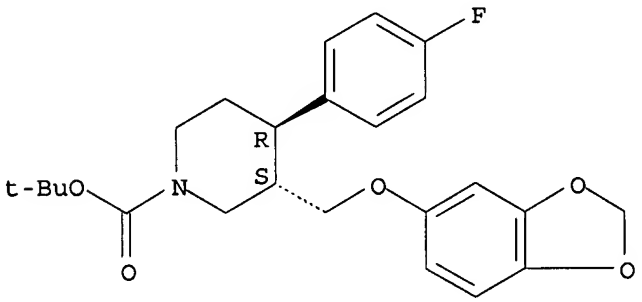
93937 REFERENCES IN FILE CAPLUS (1907 TO DATE)
24 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

tartaric acid

L8 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN 200572-35-6 REGISTRY
ED Entered STN: 29 Jan 1998
CN 1-Piperidinecarboxylic acid, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, 1,1-dimethylethyl ester, (3S,4R)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1-Piperidinecarboxylic acid, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, 1,1-dimethylethyl ester, (3S-trans)-
OTHER NAMES:
CN (3S,4R)-3-[(1,3-Benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-1-piperidinecarboxylic acid 1,1-dimethylethyl ester
FS STEREOSEARCH
MF C24 H28 F N O5
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).



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13 REFERENCES IN FILE CA (1907 TO DATE)
13 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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(110429-35-1/RN)

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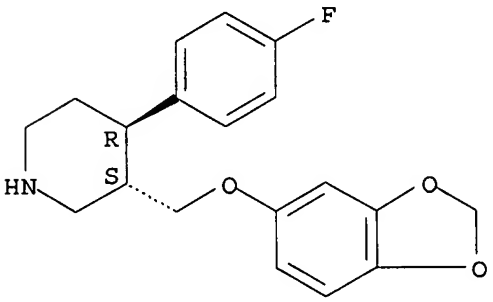
L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN 110429-35-1 REGISTRY
ED Entered STN: 27 Sep 1987
CN Piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, hydrochloride, hydrate (2:2:1), (3S,4R)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, hydrochloride, hydrate (2:1), (3S-trans)-
CN Piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, hydrochloride, hydrate (2:1), (3S,4R)- (9CI)
OTHER NAMES:
CN (-)-trans-4-(4-Fluorophenyl)-3-(3,4-methylenedioxyphenoxymethyl)piperidine hydrochloride hemihydrate
CN Paroxetine hydrochloride hemihydrate
FS STEREOSEARCH
MF C19 H20 F N O3 . Cl H . 1/2 H2 O
CI COM

tartaric acid

SR CA
LC STN Files: BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, IMSPATENTS, IMSRESEARCH, MRCK*, PS, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
CRN (61869-08-7)

Absolute stereochemistry. Rotation (-).



● HCl

● 1/2 H_2O

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

58 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
58 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> fil caplus

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FULL ESTIMATED COST	6.30	101.24

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CA SUBSCRIBER PRICE	0.00	-12.48

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